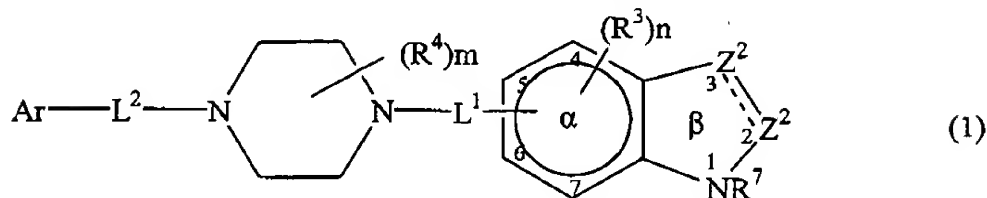


CLAIMS AMENDMENT

1. (currently amended): A compound of the formula:



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

--- represents a single or double bond;

one Z^2 is CA or CR^8A and the other is CR^1 , CR^2 , NR^6 or N wherein each R^1 , R^6 and R^8 is independently hydrogen or noninterfering substituent;

A is $-W_i-CO-X_jY$ wherein Y is COR^2 or an isostere thereof and wherein R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6 Å which is substituted or unsubstituted alkylene, alkenylene or alkynylene, or Y is tetrazole; 1,2,3-triazole; 1,2,4-triazole; or imidazole and each of i and j is independently 0 or 1;

R^7 is H or is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO_2R , RCO, COOR, alkyl-COR, SO_3R , $CONR_2$, SO_2NR_2 , CN, CF_3 , NR_2 , OR, alkyl-SR, alkyl-SOR, alkyl- SO_2R , alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl- $CONR_2$, or R_3Si , wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof;

each R^3 is independently a noninterfering substituent;

n is 0-3;

~~each of L^1 is CO, CHOH or CH_2 ; [[and]]~~

L^2 is ~~independently~~ alkylene (1-4C) or alkenylene (1-4C) alkenylene (2-4C) optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two substituents ~~on L^1 or~~ on L^2 can be joined to form a non-aromatic saturated or unsaturated

ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety;

each R^4 is independently a noninterfering substituent;

m is 0-4;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two adjacent noninterfering substituents can form a fused ring of 3-8 members; and

~~the distance between the atom of Ar linked to L^2 and the center of the α ring is 4.5-24 Å.~~

2. (original): The compound of claim 1 wherein A is COX_jCOR^2 , and wherein R^2 is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, OR, NR_2 , OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCOR_2$, CN, COOR, $CONR_2$, COR, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R^2 is OR, NR_2 , SR, $NRCONR_2$, $OCOR_2$, or $NRSO_2NR_2$, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR_2 , OCOR, NRCOR, $NRCONR_2$, $NRSO_2R$, $NRSO_2NR_2$, $OCOR_2$, or R_3Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined; and

X, if present, is alkylene.

3-4. (canceled)

5. (original): The compound of claim 1 wherein each of i and j is 0.

6. (original): The compound of claim 2 wherein j is 0.

7-8. (canceled)

9. (previously presented): The compound of claim 1 wherein R^7 is H, or is optionally substituted alkyl, or acyl.

10-11. (canceled)

12. (currently amended): The compound of ~~claim 11~~ claim 1 wherein L^1 is CO.

13-15. (canceled)

16. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted alkylene and L^1 is CO.

17. (previously presented): The compound of claim 1 wherein L^2 is unsubstituted methylene, methylene substituted with alkyl, or $-CH=$ and L^1 is alkylene or CO.

18. (original): The compound of claim 1 wherein Ar is optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof, and wherein two of said optional substituents on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

19. (original): The compound of claim 18 wherein Ar is optionally substituted phenyl.

20. (original): The compound of claim 19 wherein said optional substitution is by halo, OR, or alkyl.

21. (original): The compound of claim 20 wherein said phenyl is unsubstituted or has a single substituent.

22. (original): The compound of claim 1 wherein R^4 is selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR, $NRCONR_2$, $NRCOOR$, $OCONR_2$, RCO, COOR, alkyl-OOR, SO_3R , $CONR_2$, SO_2NR_2 , $NRSO_2NR_2$, CN, CF_3 , R_3Si , and NO_2 , wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R^4 on adjacent positions can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members, or R^4 is =O or an oxime, oximeether, oximeester or ketal thereof.

23. (original): The compound of claim 22 wherein each R^4 is halo, OR, or alkyl.

24. (original): The compound of claim 23 wherein m is 0, 1, or 2.

25. (original): The compound of claim 24 wherein m is 2 and both R^4 are alkyl.

26. (original): The compound of claim 1 wherein each R^3 is halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or NR_2 , wherein R is H, alkyl, aryl, or heteroforms thereof.

27. (original): The compound of claim 26 wherein R^3 is halo or alkoxy.

28. (original): The compound of claim 27 wherein n is 0, 1 or 2.

29. (original): The compound of claim 1 wherein L^1 is coupled to the α ring at the 4-, 5- or 6-position.

30. (previously presented): The compound of claim 1 wherein Z^2 at position 3 is CA or CHA.

31. (original): The compound of claim 30 wherein the Z^2 at position 2 is CR^1 or CR^1_2 .


32. (original): The compound of claim 31 wherein R^1 is hydrogen, or is alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR, NR_2 , SR, SOR, SO_2R , OCOR, NRCOR,

NRCONR₂, NRCOOR, OCONR₂, RCO, COOR, alkyl-OOR, SO₃R, CONR₂, SO₂NR₂, NRSO₂NR₂, CN, CF₃, R₃Si, and NO₂, wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof and two of R¹ can be joined to form a fused, optionally substituted aromatic or nonaromatic, saturated or unsaturated ring which contains 3-8 members.

33. (original): The compound of claim 32 wherein each R¹ is selected from the group consisting of H, alkyl, acyl, aryl, arylalkyl, heteroalkyl, heteroaryl, halo, OR, NR₂, SR, NRCOR, alkyl-OOR, RCO, COOR, and CN, wherein each R is independently H, alkyl, or aryl or heteroforms thereof.

34. (original): The compound of claim 30 wherein Z² at position 2 is N or NR⁶.

35. (original): The compound of claim 34 wherein R⁶ is H, or alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO₂R, RCO, COOR, alkyl-COR, SO₃R, CONR₂, SO₂NR₂, CN, CF₃, or R₃Si wherein each R is independently H, alkyl, alkenyl or aryl or heteroforms thereof.

36. (original): The compound of claim 1 wherein  represents a double bond.

37. (original): The compound of claim 1 wherein the distance between the atom on Ar linked to L² and the center of the α ring is 7.5-11Å.

38. (canceled)

39. (previously presented): A pharmaceutical composition for treating conditions characterized by enhanced p38- α activity which composition comprises a therapeutically effective amount of a compound claim 1 or the pharmaceutically acceptable salts thereof, along with a pharmaceutically acceptable excipient.

40. (withdrawn): The composition of claim 39 which further contains an additional therapeutic agent.

41. (withdrawn): The composition of claim 40 wherein said additional therapeutic agent is a corticosteroid, a monoclonal antibody, or an inhibitor of cell division.

42. (previously presented): A method to treat rheumatoid arthritis comprising administering to a subject in need of such treatment a compound of claim 1 or the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof.

43-44. (canceled)

45. (previously presented): The compound of claim 36, wherein Z^2 at position 3 is CA.

46. (previously presented): The compound of claim 45, wherein Z^2 at position 2 is CR¹.

47. (previously presented): The compound of claim 46, wherein A is COCOR².

48. (previously presented): The compound of claim 47, wherein R² is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, OR, NR₂, OCOR, NRCOR, NRCONR₂, NRSO₂R, NRSO₂NR₂, OCONR₂, CN, COOR, CONR₂, COR, or R₃Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, or

wherein R² is OR, NR₂, SR, NRCONR₂, OCONR₂, or NRSO₂NR₂, wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, heteroarylalkyl, each optionally substituted with halo, SR, OR, NR₂, OCOR, NRCOR, NRCONR₂, NRSO₂R, NRSO₂NR₂, OCONR₂, or R₃Si wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom-containing forms thereof wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined.

49. (previously presented): The compound of claim 48, wherein R¹ is H.

50. (previously presented): The compound of claim 49, wherein n is 0 or 1.
51. (previously presented): The compound of claim 50, wherein Ar is substituted phenyl.
52. (previously presented): The compound of claim 51, wherein L^2 is unsubstituted or substituted alkylene optionally including a heteroatom.
53. (previously presented): The compound of claim 52, wherein L^1 is alkylene or CO.
54. (previously presented): The compound of claim 53, wherein L^2 is methylene and L^1 is CO.
55. (previously presented): The compound of claim 54, wherein n is 1 and R^3 is halo or methoxy.
56. (previously presented): The compound of claim 55, wherein R^7 is H or alkyl.
57. (previously presented): The compound of claim 56, wherein R^7 is methyl.
58. (previously presented): The compound of claim 57, wherein Ar is para-fluorophenyl.
59. (previously presented): The compound of claim 58, wherein R^2 is OR, NR_2 , SR, $NRCONR_2$, $OCONR_2$ or $NRSO_2NR_2$ wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom containing forms thereof and wherein two R attached to the same atom may form a 3-8 membered ring.
60. (previously presented): The compound of claim 59, wherein R^2 is NR_2 wherein each R is independently H, alkyl, alkenyl or aryl or the heteroatom containing forms thereof and wherein two R attached to the same atom may form a 3-8 membered ring.

61. (previously presented): The compound of claim 60, which is selected from the group consisting of compound Nos. 15, 33, 57, 59, 77, 89, 96, and 100 of Table 2, *i.e.*,

1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide;

1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide;

1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide; and

1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

62. (previously presented): The compound of claim 60, wherein said compound is compound No. 15 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

63. (previously presented): The compound of claim 60, wherein said compound is compound No. 33 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

64. (previously presented): The compound of claim 60, wherein said compound is compound No. 57 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

65. (previously presented): The compound of claim 60, wherein said compound is compound No. 59 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalicamide.

66. (previously presented): The compound of claim 60, wherein said compound is compound No. 77 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N-methyl-glyoxalicamide.

67. (previously presented): The compound of claim 60, wherein said compound is compound No. 89 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

68. (previously presented): The compound of claim 60, wherein said compound is compound No. 96 of Table 2, *i.e.*, 1-methyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

69. (previously presented): The compound of claim 1, wherein said compound is compound No. 162 of Table 2, *i.e.*, 6-chloro-[4'-fluoro-(4-benzyl-2,5-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

70. (previously presented): The compound of claim 60, wherein said compound is compound No. 100 of Table 2, *i.e.*, 1-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

71. (previously presented): The compound of claim 1, wherein said compound is compound No. 17 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

72. (previously presented): The compound of claim 1, wherein said compound is compound No. 38 of Table 2, *i.e.*, 1-ethoxycarbonyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

73. (previously presented): The compound of claim 1, wherein said compound is compound No. 45 of Table 2, *i.e.*, 1-*t*-butoxycarbonyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

74. (previously presented): The compound of claim 1, wherein said compound is compound No. 56 of Table 2, *i.e.*, 1-acetyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

75. (previously presented): The compound of claim 1, wherein said compound is compound No. 60 of Table 2, *i.e.*, 1-acetyl-2-methyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

76. (previously presented): The compound of claim 1, wherein said compound is compound No. 63 of Table 2, *i.e.*, 1-methoxymethyl-6-chloro-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

77. (previously presented): The compound of claim 1, wherein said compound is compound No. 92 of Table 2, *i.e.*, 1-methoxymethyl-6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperazinyl)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

78. (previously presented): The compound of claim 1, wherein said compound is compound No. 102 of Table 2, *i.e.*, 1-methyl-6-chloro-[4-(1-4'-fluorophenylethyl)piperazinyl]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

79. (previously presented): The compound of claim 1, wherein said compound is compound No. 137 of Table 3, *i.e.*, 6-methoxy-(4-benzyl piperazinyl)-indole-5-carboxamide-3-glyoxalic acid-methyl ester.

80. (previously presented): The compound of claim 1, wherein said compound is compound No. 138 of Table 3, *i.e.*, [4-(1-phenylethyl)piperazinyl]-indole-5-carboxamide-3-glyoxalic acid methyl ester.

81. (previously presented): The compound of claim 1, wherein said compound is compound No. 152 of Table 3, *i.e.*, (4-benzyl-2R,5S-piperaziny)-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

82. (previously presented): The compound of claim 1, wherein said compound is compound No. 161 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2,5-dimethyl piperaziny)]-indole-5-carboxamide-3-glyoxalic acid-morpholinamide.

83. (previously presented): The compound of claim 1, wherein said compound is compound No. 177 of Table 3, *i.e.*, 6-methoxy-[4'-fluoro-(4-benzyl-2R,5S-dimethyl piperaziny)]-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.

84. (previously presented): The compound of claim 1, wherein said compound is compound No. 180 of Table 3, *i.e.*, (6-methoxy[4-(1-4'-fluorophenylethyl)piperaziny])-indole-5-carboxamide-3-N,N-dimethyl glyoxalicamide.